

**Notice of Allowability**

Application No.

10/698,106

Examiner

Christina Marchetti Bradley

Applicant(s)

ROBOTTI, KARLA M.

Art Unit

1654

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the after-final amendment filed 10/23/2006.
2. ☐ The allowed claim(s) is/are 1,3,4,6-8,18-21 and 38.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of the:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |  |   |
|--|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)   | 5. <input type="checkbox"/> Notice of Informal Patent Application                     |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____ |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date _____    | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment                   |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material | 8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance             |
|  | 9. <input type="checkbox"/> Other _____   |

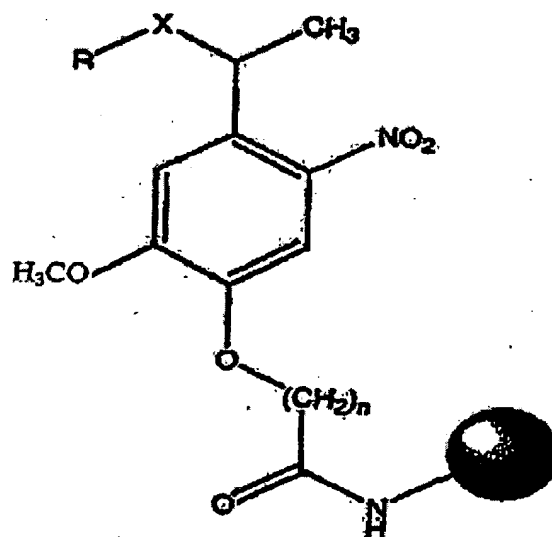
**EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Christopher Linder on 11/17/2006.

The application has been amended as follows:

1. A method of separating phosphorylated peptides from a mixture comprising phosphorylated peptides and unphosphorylated peptides, comprising the steps of:
  - a) reacting a collection of peptides with a non-magnetic first resin, wherein some of the peptides have one or more phosphate groups, wherein the first resin is a photocleavable resin represented by the following structural formula:



wherein,

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n is an integer,

X is -NH-,

R is -H, or an amino acid, a peptide, an isotope labeled amino acid, or an isotope labeled peptide with a primary or secondary amine,

and shaded circle is a bead, a pallet, a disk, capillary, a hollow fiber, a needle, a membrane, a solid fiber, a cellulose bead, a polystyrene bead, a grafted co-polymer bead, a poly-acrylamide bead, a latex bead, a dimethylacrylamide bead, or combinations thereof;

wherein the primary or secondary amine groups represented by X and/or R react with the carboxylic acid groups of the peptides to form an amide bond and the phosphate groups of the peptides to form a phosphoramidate bond; thereby forming a first collection of peptides comprising unphosphorylated peptides with first resin bound carboxylic groups and phosphorylated peptides with first resin bound carboxylic acid and phosphate groups;

b) selectively cleaving the first resin that reacted with the phosphate groups of the phosphorylated peptides to regenerate the phosphate groups, thereby forming a second collection of peptides comprising unphosphorylated peptides with first resin bound carboxylic groups and phosphorylated peptides with first resin bound carboxylic acid groups;

c) reacting the phosphate groups of the second collection of peptides with a second resin to form a bond between the phosphorylated peptides and the second resin, wherein the second resin comprises an amino acid residue with a primary or secondary amine group, and wherein the second resin is magnetic, thereby forming a third collection of peptides comprising unphosphorylated peptides with first resin bound carboxylic groups and phosphorylated peptides with first resin bound carboxylic acid groups and second resin bound phosphate groups;

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d) selectively cleaving the first resin by exposing the third collection of peptides to light, thereby forming a fourth collection of peptides comprising unphosphorylated peptides that are not bound to a resin and phosphorylated peptides that are bound to the second resin;

e) separating phosphorylated peptides from unphosphorylated peptides by exposing the fourth collection of peptides to a magnetic field and separating the peptides that are not bound to a resin from peptides that are bound to the second resin, thereby forming a fifth collection of peptide comprising phosphorylated peptides that are bound to the second resin.

2. cancelled

3. The method of claim 1, further comprising the step of cleaving the bond between the second resin and the phosphorylated peptides in the fifth collection of peptides to form unbound phosphorylated peptides.

4. The method of claim 1, further comprising the step of reacting the peptides with a reagent for protecting amine groups before reacting the peptides with the first resin.

5. cancelled

6. The method of claim 1, wherein the phosphoramidate bonds are selectively cleaved in step b) by contacting the first collection of peptides with a weak acid or a weak base.

7. The method of claim 1, wherein R is a peptide or an amino acid residue, wherein the peptide or amino acid residue has a primary or secondary amine group.

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8. The method of claim 7, wherein the peptide or amino acid residue is isotope labeled, and wherein the isotope labeled peptide or amino acid residue remains bound to the peptide when the first resin is selectively cleaved.

9. cancelled

10. cancelled

11-17. cancelled

18. The method of claim 38, further comprising contacting the fourth collection of peptides with an affinity resin, wherein the affinity resin comprises a second recognition entity of the molecular recognition system bound to a solid support, thereby binding the peptides bound to the first recognition entity to the affinity resin.

19. The method of claim 18, wherein the molecular recognition system comprises an antigen/antibody, an antigen/antibody fragment, an avidin/biotin, a streptavidin/biotin, a protein A/I<sub>g</sub> or a lectin/carbohydrate.

20. The method of claim 18, wherein the affinity resin is collected by filtration, thereby separating phosphorylated peptides from unphosphorylated peptides.

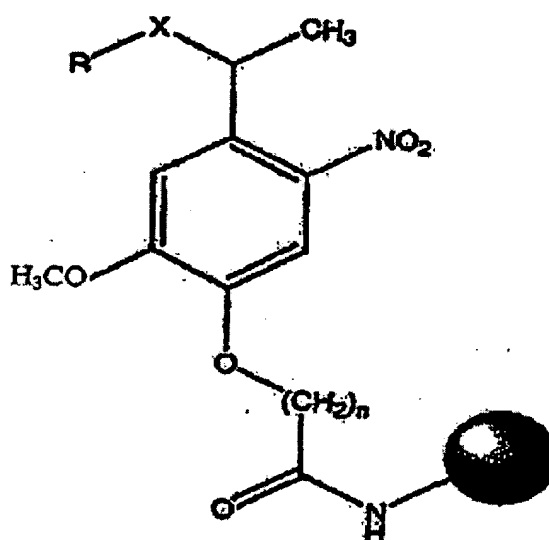
21. The method of claim 18, wherein the fourth collection of peptides is passed through a column comprising the affinity resin, thereby separating phosphorylated peptides from unphosphorylated peptides.

22-37. cancelled

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38. A method of separating phosphorylated peptides from a mixture comprising phosphorylated peptides and unphosphorylated peptides, comprising the steps of:

a) reacting a collection of peptides with a non-magnetic first resin, wherein some of the peptides have one or more phosphate group, wherein the first resin is a photocleavable resin represented by the following structural formula:



wherein,

n is an integer,

X is -NH-,

R is -H, or an amino acid, a peptide, an isotope labeled amino acid, or an isotope labeled peptide with a primary or secondary amine,

and shaded circle is a bead, a pallet, a disk, capillary, a hollow fiber, a needle, a membrane, a solid fiber, a cellulose bead, a polystyrene bead, a grafted co-polymer bead, a poly-acrylamide bead, a latex bead, a dimethylacrylamide bead, or combinations thereof;

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wherein the primary or secondary amine groups represented by X and/or R react with the carboxylic acid groups of the peptides to form an amide bond and the phosphate groups of the peptide to form a phosphoramidate bond; thereby forming a first collection of peptides comprising unphosphorylated peptides with first resin bound carboxylic groups and phosphorylated peptides with first resin bound carboxylic acid and phosphate groups;

b) selectively cleaving the first resin that reacted with the phosphate groups of the phosphorylated peptides to regenerate the phosphate groups, thereby forming a second collection of peptides comprising unphosphorylated peptides with first resin bound carboxylic groups and phosphorylated peptides with first resin bound carboxylic acid groups;

c) reacting the phosphate groups of the second collection of peptides with a capture ligand to form a bond between the phosphorylated peptides and the capture ligand, wherein the capture ligand is a first recognition entity of a molecular recognition system; thereby forming a third collection of peptides comprising unphosphorylated peptides with first resin bound carboxylic groups and phosphorylated peptides with first resin bound carboxylic acid groups and capture ligand bound phosphate groups;

d) selectively cleaving the first resin by exposing the third collection of peptides to light, thereby forming a fourth collection of peptides comprising unphosphorylated peptides that are not bound to a resin and phosphorylated peptides that are bound to the capture ligand;

e) separating peptides bound to the capture ligand from peptides that are not bound to the capture ligand, thereby separating phosphorylated peptides from unphosphorylated peptides.

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Support for the amendment to the claims can be found in Figures 2 and 3.

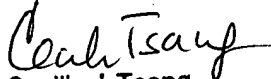
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571) 272-9044. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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